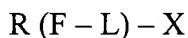


IN THE CLAIMS

Please amend claims 12, 14 and 23 as rewritten below. The following listing of claims replaces all prior listings.

1. (Withdrawn) A composition comprising at least one covalent product of a target enzyme of a complex protein composition and at least one activity based probe member of a combinatorial chemical library comprising a plurality of members of the formula



wherein:

X is a ligand, said ligand having the same chemical structure for each of said members of said library;

L is a bond or linking group, which is the same in each of the members of said library, and said linking group is of from 1 to 20 carbon atoms;

F is a sulphonyl group reactive at an active site of a target enzyme; and

R is an organic group of less than 1kDal, that is different in each of the members of the library and is bonded to F; and

wherein members of the library have different on rates with said target enzyme.

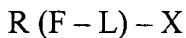
2. (Withdrawn) A composition according to Claim 1, wherein R is selected from the group consisting of alkyl, cycloalkyl, heterocycle and aryl and substituted members thereof.

3. (Withdrawn) A composition according to claim 1, wherein said target enzyme is an aldehyde dehydrogenase.

4. (Withdrawn) A composition according to Claim 1, wherein said linking group is an aliphatic chain.

5. (Withdrawn) A composition according to Claim 1, wherein said linking group is an alkyleneoxy chain of from one to 6 alkyleneoxy groups, wherein said alkyleneoxy is of from 2 to 3 carbon atoms.

6. (Withdrawn) A compound of the formula:



wherein:

X is biotin;

L is alkylene or an alkyleneoxy chain of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms;

F is a sulphonyl group

R is heteroaryl or aryl.

7. (Withdrawn) A compound according to Claim 6, wherein R is pyridyl.

8. (Withdrawn) A compound according to Claim 6, wherein R is thiophenyl.

9. (Withdrawn) A combinatorial chemical library comprising a plurality of members of the formula R (F - L) - X

wherein:

X is a ligand for binding to a reciprocal receptor;

L is alkylene or an alkyleneoxy chain of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms;

F is a sulphonyl group reactive at an active site of a target enzyme; and

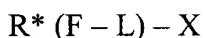
R is an organic group of less than 1kDa, that is different in each of the members of the library and is bonded to R; and

wherein members of the library have different on rates with said target enzyme.

10. (Withdrawn) A combinatorial library according to Claim 9, wherein R in one member of said library is pyridyl or thiophenyl.

11. (Withdrawn) A combinatorial library according to Claim 9, wherein said ligand is biotin.

12. (Currently amended) A method for screening for molecules having an affinity for an active protein in a complex mixture of proteins from a biological source, employing a combinatorial chemical library comprising a plurality of members of the formula



wherein:

X is a ligand having the same chemical structure for each of said members of said combinatorial chemical library,

L is a bond or alkylene or an alkyleneoxy chain linking group of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms, which is the same in each of the members of said combinatorial chemical library;

F is a sulfonyl functional group reactive at an active site of a protein member, which functional group comprises the same reactive functionality in each of the members of said combinatorial chemical library, and

R is a group of less than 1kDal, that is different in each of the members of the combinatorial chemical library;

the * intends that R is a part of F or L; and

wherein members of said combinatorial chemical library have different on rates with said protein member; said method comprising:

(1) combining with said complex mixture of proteins, in an active form and an inactivated form, said combinatorial chemical library under conditions for reaction of said sulfonyl functional group with active proteins to form a conjugate;

(2) isolating conjugates from said active and inactivated complex mixture of proteins; and

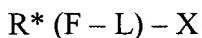
(3) comparing conjugates formed with said active and inactivated complex mixtures of proteins;

whereby conjugates in said active complex mixture absent in said inactivated complex mixture are comprised only of active proteins reactive with members of said chemical combinatorial library.

13. (Withdrawn) A method according to Claim 12, wherein each of said members of said combinatorial library is isotopically individually labeled, said method including the additional steps of:

isolating conjugates from said active complex mixtures; and
analyzing said conjugates for the composition of said probe by means of said isotopic individual label and for the composition of said protein by at least partial sequencing.

14. (Currently amended) A method for screening for molecules having an affinity for an active target protein in a complex mixture of proteins from a biological source, employing a combinatorial chemical library of activity based probes comprising a plurality of members of the formula



wherein:

X is a ligand having the same chemical structure for each of said members of said combinatorial chemical library;

L is a bond or alkylene or an alkyleneoxy chain linking group of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms, which is the same in each of the members of said combinatorial chemical library,

F is a sulfonyl group that is the same in each member of said combinatorial chemical library; and

R is a group of less than 1kDal, that is different in each of the members of the combinatorial chemical library;

the * denotes that R is a part of F or L;

said method comprising:

(1) combining a first portion of said complex mixture of proteins with said combinatorial chemical library under conditions for reaction of said sulfonyl group with active proteins in said complex mixture of proteins to form conjugates;

(2) combining a second portion of said complex mixture of proteins, that has been inactivated, with said combinatorial library under the same reaction conditions as in (1)

(3) isolating conjugates from said first and second portions of said complex mixture of proteins; and

(4) comparing conjugates formed from said first portion of said complex mixture of proteins with conjugates formed from said second portion of said complex mixture of proteins to determine the degree of activity of the total target protein as compared to active target protein.

15. (Withdrawn) A method according to claim 14, wherein each of said members of said combinatorial chemical library of activity based probes is isotopically labeled, said method including the additional step of analyzing said conjugates for the composition of proteins bound to members of said library.

16. (Previously added) A method according to claim 14, wherein said members of said combinatorial chemical library of activity based probes have differing on-rates with respect to said active proteins.

17. (Previously added) A method according to claim 14, wherein X is biotin, deiminobiotin, dethiobiotin, a vicinal diol, digoxigenin, maltose, oligohistidine, glutathione, 2,4-dinitrobenzene, phenylarsenate, ssDNA, ds DNA, a peptide, metal chelate, saccharide, rhodamine, fluorescein, or a hapten.

18. (Previously added) A method according to claim 14, wherein X is biotin.
19. (Withdrawn) A method according to claim 14, wherein X is rhodamine.
20. (Previously added) A method according to claim 14, wherein R is alkyl, heterocyclic, aryl, substituted aryl, amino acid, peptidyl, oligonucleotide, or a carbohydrate group.
21. (Previously added) A method according to claim 14, wherein F is sulfonate, sulfate, sulfinate, or sulfamate.
22. (Previously added) A method according to claim 21, wherein F is sulfonate.
23. (Currently amended) A method according to claim 14, wherein said second portion of said complex proteomic mixture of proteins has been inactivated by heating.
24. (Previously added) A method according to claim 14, wherein said combinatorial chemical library of activity based probes comprises at least two of sulfonate 1 - sulfonate 11 and sulfonate 15 - sulfonate 17.